

## **REMARKS**

### **Status of the Claims**

Claims 1 and 3-8 are pending in the present application. Claims 9-12 are withdrawn as being directed to a non-elected invention. Claim 1 is amended. Support for amended claim 1 is found in original claim 2, now canceled, and throughout the application as originally filed including on pages 3-4, bridging paragraph, and page 14, paragraphs 2-3. Claim 1 is also amended to define the acronym, "ABC." Claims 3, 4, 7, and 8 are amended to correct typographical errors, antecedent basis and/or define acronyms. No new matter has been added by way of this amendment. Reconsideration is respectfully requested.

### **Claim Objections**

The Examiner objects to claims 1, 3, 7, and 8 because of several informalities. In order to overcome this objection, Applicants have amended claims 1, 3, 7, and 8 in order to correct the deficiencies pointed out by the Examiner. In view of the amendments, withdrawal of the objections is respectfully requested.

### **Issue Under 35 U.S.C. § 112, 2nd Paragraph**

Claims 1-8 stand rejected under 35 U.S.C. § 112, 2nd Paragraph. This rejection is respectfully traversed.

The Examiner has set forth certain instances wherein the claim language lacks antecedent basis or is not clearly understood.

In order to overcome this rejection, Applicants have amended claims 1, 3, 4, and 7 to correct each of the deficiencies specifically pointed out by the Examiner. Applicants respectfully submit that the claims, as amended, particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Further, in response to the Examiner's allegation that claim 1 omits essential steps, Applicants have amended claim 1 to specify that the method comprises measuring the presence or absence of amplification of the ABC transporter gene in said test cancer cell, wherein said ABC gene is an A3(ABCA3) gene, and judging that said test cancer cell has acquired a drug resistance to etoposides when amplification of the ABCA3 gene is detected in said test cancer cell.

With respect to the further rejection of claim 7, Applicants submit that the claim is not unclear. An ordinary artisan would understand from the claim that the fluorescent dye described in line 7 of claim 7 is obtained as a result of hybridization.

In view of the foregoing amendments, Applicants believe the rejections are overcome and respectfully request withdrawal.

### **Issue under 35 U.S.C. §103**

Claims 1-8 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Watts, *The Journal of Pharmacology and Experimental Therapeutics*, 2001, 299:434, ("Watts"), in combination with Efferth, *Current Molecular Medicine*, 2001, 1:45, ("Efferth"), in further view of Wessendorf, *Laboratory Investigation*, 2002, 82:47, ("Wessendorf"). This rejection is respectfully traversed.

As amended, independent claim 1 is directed to a detection method of detecting acquisition of a drug resistance of a test cancer cell to etoposides, which comprises detecting the presence or absence of amplification of an ATP binding cassette (ABC) transporter gene in said test cancer cell by measuring the presence or absence of amplification of the ABC transporter gene in said test cancer cell, wherein said ABC gene is an A3(ABCA3) gene, and judging that said test cancer cell has acquired a drug resistance to etoposides when amplification of the ABCA3 gene is detected in said test cancer cell.

Applicants submit that none of the cited references, either alone or in combination, teach or suggest all of the elements of independent claim 1. Watts discloses that the MDR1 gene, which is also known as the ABCB1 gene, is involved in doxorubicin resistance. However, Watts does not teach or suggest the association of amplification of the ABCA3 gene with etoposide resistance.

Tables 1 and 2 of Efferth recite the ABCA3 gene. In particular, Tables 1 and 2 of Efferth, describe the ABCA3 gene simply as one type of ABC transporter. That is, Efferth does not teach or suggest that the ABCA3 gene is involved in drug resistance, especially in etoposide drug resistance. Instead, Efferth describes that the ABCC1(MRP1) gene is involved in drug resistance of tumors, and that the ABCB1 gene is involved in the drug resistance of cancer, *see* page 51 and pages 48-50 of Efferth, respectively. Efferth further discloses that some ABC transporter genes are involved in drug resistance. However, as noted above, Efferth does

not identify this association with the ABCA3 gene. In view of the foregoing, Applicants submit that an ordinary artisan would not have been motivated to combine Watts with Efferth. Further, even if Watts were combined with Efferth, this combination does not describe that the ABCA3 gene is involved in etoposide resistance. Wessendorf fails to remedy the deficiencies of Watts and Efferth since Wessendorf is merely cited for teaching the elements of dependent claim 8.

In view of the foregoing, none of the cited references, either alone or in combination, teach all of the elements of independent claim 1 or dependent claims 3-8, which incorporate all of the elements of independent claim 1. Accordingly, the claims are not rendered obvious by the cited references. Withdrawal of the rejection is respectfully requested.

### **CONCLUSION**

In view of the above amendment and remarks, Applicants believe the pending application is in condition for allowance.


Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact L. Parker, PhD, Registration No. 46,046, at the telephone number of the undersigned below to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Director is hereby authorized in this, concurrent, and future replies to charge any fees required during the pendency of the above-identified application or credit any overpayment to Deposit Account No. 02-2448.

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Respectfully submitted,

By



Marc S. Weiner

Registration No.: 32181

BIRCH, STEWART, KOLASCH & BIRCH, LLP

8110 Gatehouse Road, Suite 100 East

P.O. Box 747

Falls Church, VA 22040-0747

703-205-8000

**GARTH M. DAHLEN**  
USPTO #43,575